The following amendment and remarks are submitted In response to the May 26, 2004 Office Action.

Enclosed is a check for $490 for a three-month extension of time for a small entity, to extend the time for response from August 26, 2004 to November 26, 2004 (37 C.F.R. § 1.136(a)(3)). If this amount is incorrect, please refer to the Deposit Account Authorization previously filed with this application. If any additional extension of time is required, please consider this paper a petition for the total extension of time required.

In the Specification:

Please add the following paragraph to page 1, before paragraph **[0001]**:

> The benefit of the February 23, 2001 filing date of provisional application serial number 60/271,286 is claimed under 35 U.S.C. §119(e).

Remarks:

Claims 1-10 remain in the application. The Specification has been amended to claim priority to a provisional application under 35 U.S.C. §119(e). This priority was claimed in the Application Data Sheet filed with the current application on February 22, 2001.

The §112, First Paragraph, Rejections

Claims 1, 4, and 6-10; and Written Description

Claims 1, 4, and 6-10 were rejected under 35 U.S.C. §112, first paragraph, as having an inadequate written description. In particular, the Office found an insufficient description for the functional term "a bFGF-active PAF antagonist."

The MPEP §2163 (pg. 2100-163) states that "[t]here is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed." In the same paragraph, the MPEP states that "rejection of an original claim for lack of written description should be rare." In a later part of the same section, pg. 2100-165,

the MPEP states that "[a] specification may describe an actual reduction to practice by showing that the inventor constructed an embodiment or performed a process that met all the limitations of the claim and determined that the invention would work for its intended purpose."

Applicants respectfully submit that the term "a bFGF-active PAF antagonist" as used in the Claims is adequately described in the Specification. The term is defined in the Specification, page 7, paragraph [0030], as: "a PAF antagonist that binds to the intracellular PAF binding sites and inhibits angiogenesis otherwise stimulated by bFGF." Persons skilled in the art would clearly understand this definition based on the contents of this specification and the literature in the field. Moreover, the Specification and the Claims recite two examples of a PAF antagonist that are known in the literature to bind the intracellular PAF binding site in the literature, i.e., BN-50730 and CV3988. See Specification, page 3-4, paragraph [0007]. The structure of BN-50730 is shown in Fig. 1. Additionally, the specification describes an actual reduction of practice of an embodiment that indicates the Applicants were in possession of the invention as claimed. For example, the experiments described in the examples show that two different tumor types are reduced *in vivo* using BN-50730 (e.g., Example 2, paragraphs [0048]-[0052]), and that BN-50730 inhibits angiogenesis stimulated by bFGF, and not other growth factors (e.g., Example 6, paragraphs [0058]-[0060]). Given these explicit examples and given the teaching of the Specification of a whole, Applicants respectfully submit that the application contains sufficient written description to support the Claims as written.

This is NOT a case where no examples of a "bFGF -active PAF antagonist" as defined in the Specification are given. This is NOT a case where no structure of a known "bFGF-active PAF antagonist" is given. This is NOT a case in which the invention is merely a wish. This invention as claimed has been reduced to practice with a known "bFGF-active PAF antagonist" whose structure is given. Applicants respectfully submit that the specification contains a written description of the invention as claimed and that this rejection should be withdrawn.

Claims 1-8, and Enablement.

Claims 1-8 were rejected under 35 U.S.C. §112, first paragraph, for not being enabling for inhibiting tumors beyond carcinoma of the lung and prostate.

The MPEP §2164.01(b) (pg. 2100-180) states that "[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied." Moreover, "the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experiments." MPEP §2164.01.

Claim 1, the only independent claim, is NOT directed to any tumor, but specifically to tumors "wherein the *growth of the tumor depends on basic fibroblast growth factor-stimulated angiogenesis.*" Examples of such tumors are listed in Claim 8. The instant application describes the novel finding that the tumorgenic bFGF angiogenic pathway involves PAF and can be inhibited by PAF antagonists but only those that bind to intracellular PAF binding sites. See, for example, Specification, paragraphs [0010] and [0029]. The term "bFGF-active PAF antagonist" is specifically defined, as shown above, as "a PAF antagonist that binds to the intracellular PAF binding sites and inhibits angiogenesis otherwise stimulated by bFGF." Applicants respectfully submit that Claim 1 is not overly broad based on the description of the technology in the Specification. Two working examples are described in detail that show two different human tumor types to be affected by the bFGF-active PAF antagonist, BN-50730, in Example 2, paragraphs [0048]-[0052]. Moreover, the Specification includes explicit experimental protocols for prospective experiments on the tumor types listed in Claim 8. Experimental protocols that are routine to a person skilled in the art. See, Specification, paragraph [0052] (based on protocol described in Examples 1 and 2), and Example 9, paragraphs [0065]-[0066].

If the factors of enablement are considered, Applicants submit that the Specification as written fully enables a person skilled in the art to make and use the invention. Applicants submit that the invention as claimed does not require undue experimentation.

(1) The nature of the invention: The invention as claimed in Claim 1 is directed to:

> A method of inhibiting the growth of a tumor in a mammal, wherein the growth of the tumor depends on basic fibroblast growth factor-stimulated angiogenesis, said method comprising administering to the mammal a therapeutically effective amount of a bFGF-active PAF antagonist.

Applicants were the first to report that a PAF antagonist caused a significant reduction in angiogenesis and tumor growth in tumor models which stimulate angiogenesis using bFGF. Claim 1 does not include ANY tumor but only tumors whose growth depends on bFGF-stimulated angiogenesis. In addition, Claim 1 does not include ANY PAF antagonist but only those that fit the definition of a "bFGF-active PAF antagonist." The Specification discloses an explicit experiment to show decrease in tumor size in two separate human tumor types (lung carcinoma and prostate carcinoma) due to a bFGF-active PAF antagonist (Example 2). Moreover, using human HUVEC cells, Example 6 (paragraphs [0058]-[0060]), applicants demonstrated that the angiogenesis was inhibited by the PAF antagonist BN-50730 when stimulated by bFGF, but not by other tested growth factors. Thus the specification gives considerable guidance of methods to practice the invention as claimed.

(2) The state of the prior art: As described in the Specification, for example, paragraphs [0008] and [0029], the prior art had reported that bFGF-stimulated angiogenesis was PAF independent, in contrast to the findings by applicants. Applicants were the first to report that a PAF antagonist caused a significant reduction in angiogenesis and tumor growth in tumor models which stimulate angiogenesis using bFGF. The prior art describes several PAF antagonists and their location of binding. A person skilled in the art would be knowledgeable on how to find PAF antagonists that bind to intracellular receptors.

(3) As indicated by the Office, the relative skill of those in the art is high.

(4) The predictability or unpredictability of the art. Applicants respectfully submit that this invention as described in Claim 1 is not unpredictable. The tumor is defined as one whose growth "depends on basic fibroblast growth factor stimulated angiogenesis," and the therapeutic agent is defined as "a bFGF-active PAF antagonist," which is further defined in the Specification as a "PAF antagonist that binds to the intracellular PAF binding sites and inhibits angiogenesis otherwise stimulated by bFGF." Thus Claim 1 is not overly broad and unpredictable. The Applicants give two examples of "bFGF-active PAF antagonist" and give the structure of one of the named compounds in Fig. 1.

(5) The breadth of the claims: Claim 1, the only independent claim, is the broadest claim. As described above, Claim 1 does not include ANY tumor and the bFGF-active PAF antagonist is defined and described in the Specification.

(6) The amount of direction and guidance: Applicants respectfully submit that the Office is wrong in indicating that the Specification "provides no guidance, in the way enablement for the treatment or inhibition of tumors of carcinoma of the lung and prostate." Pg. 9, May 26, 2004 Office Action. The Specification has numerous working examples that would guide a person skilled in the art on the use of this technology. For example, Examples 1 and 2 describe the use of nude mice injected with human tumor cells of both prostate and lung in an *in vivo* experiment showing the treatment and subsequent decrease in tumor growth when the bFGF-active PAF antagonist was given to the mice. Example 9 describes the use of prospective experiments using nude mice in a similar experimental protocol to Examples 1 and 2 to indicate that other tumors that depend on bFGF-stimulated angiogenesis to growth would also be decreased by application of the bFGF-active PAF antagonist. Given the high level of skill in the art, Applicants respectfully submit that the direction and guidance in the application is more than adequate to enable a person skilled in the art to make and use this invention.

(7) The presence of working examples: As described above, Applicants respectfully submit that the Specification contains sufficient working and prophetic examples to enable Claim 1 as written, for example, Examples 1, 2 and 9.

(8) The quantity of experimentation necessary: The experimentation necessary is merely routine given the guidance of the present Specification and using techniques known in the field. For instance, the use of nude mice and tumor cell lines are well known in the field. As described above, and particularly in Examples 2 and 9, the Specification contains the required amount of guidance. Applicants disagree that undue experimentation would be required given the skill in the art and current technology.

Applicants respectfully submit their application is similar to the finding by the Federal Circuit in *In re Wands,* in that the application as filed gives "considerable direction and guidance on how to practice the invention and presents working examples. There was a high level of skill in the art at the time the application was filed, and all the methods needed to practice the invention were well known." *In re Wands*, 858 F.2d 731, 740 (Fed. Cir. 1988).

Thus Applicants respectfully submit that the broadest Claim 1 is fully enabled by the current Specification, and all other claims depend from Claim 1. Applicants respectfully submit that claims 2-7 are also enabled for the above reasons, and that this rejection should be withdrawn.

The §112, Second Paragraph Rejections

Claims 1 and 4-10 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The Office stated that the claims are "directed to the administration of a functionally written compounds that are described as bFGF-active PAF antagonist compounds" and that defining a compound by its function "renders these claims vague and indefinite because this function recitation embraces compounds that are not yet synthesized."

The primary purpose of the requirement of definiteness is "to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent." MPEP §2173. As stated in the MPEP §2173.05(g), "[t]here is nothing inherently wrong with defining some part of an invention in functional terms. Functional language does not, in and of itself, render a claim improper. *In re Swinehart,* 439 F.2d 210, 169 USPQ 226 (CCPA 1971)." The MPEP further states that the functional

limitation must be evaluated for "what it conveys to a person of ordinary skill in the pertinent art in the context in which it is used." The example given in this section as one held acceptable was one defining "a radical on a chemical compound as 'incapable of forming a dye with said oxidizing developing agent' although functional, was perfectly acceptable because it set definite boundaries on the patent protection sought. *In re Barr,* 444 F.2d 588, 170 USPQ 33 (CCPA 1971)."

Applicants respectfully submit that claims 1 and 4-10 are not indefinite. Applicants respectfully submit that the term "a bFGF-active PAF antagonist" as used in the Claims is adequately defined and adequately sets boundaries on the patent protection sought. The Specification, page 7, paragraph [0030], defines this term as: "a PAF antagonist that binds to the intracellular PAF binding sites and inhibits angiogenesis otherwise stimulated by bFGF." Persons skilled in the art would clearly understand this definition based on the contents of this specification and the literature in the field. The MPEP §2173.01 recognizes that the applicants "are their own lexicographers" and can define terms using functional language as long as the claim "makes clear the boundaries of the subject matter for which protection is sought." There is nothing in the MPEP that indicates functional language is inappropriate merely because it might embrace elements not yet made. In fact, the MPEP recognizes that "breadth of a claim is not to be equated with indefiniteness." MPEP §2173.04. Applicants respectfully submit the claim language is sufficiently clear to inform the public of "what constitutes infringement of the patent." MPEP §2173.

Moreover, the Specification and the Claims recite two examples of a PAF antagonist that are known in the literature to bind the intracellular PAF binding site in the literature, i.e., BN-50730 and CV3988. See Specification, page 3-4, paragraph [0007]. Additionally, the specification describes an actual reduction of practice of an embodiment that indicates the invention as claimed will work. For example, the experiments described in the examples show that two different tumor types are reduced *in vivo* using BN-50730 (e.g., Example 2, paragraphs [0048]-[0052]), and that BN-50730 inhibits angiogenesis stimulated by bFGF, and not other growth factors (e.g., Example 6, paragraphs [0058]-[0060]). Given these explicit examples and given the teaching of the Specification of a whole, Applicants

respectfully submit that the application and the claims "set definite boundaries on the patent protection sought" and that this rejection should be withdrawn.

The §102 and §103 Rejections

Claims 1-4 and 8-10 were rejected under 35 U.S.C. §102(a) as being anticipated by Hunt *et al.*, abstract 4099, of Proceedings of the American Assoication of Cancer Research. Attached to this Amendment is an Affidavit of Jay D. Hunt (Exhibit A) that demonstrates this paper constitutes a publication of the applicants' own invention. As the abstract was published less than one year before the February 2001 filing date of the provisional application whose benefit is claimed under 35 U.S.C. § 119(e), the paper has been removed as a reference against this application. It is respectfully submitted that this ground of rejection should be withdrawn.

Claims 1-10 were rejected under 35 U.S.C. §103(a) as being unpatentable over the same abstract. In light of the Affidavit of Dr. Hunt, this reference is removed as a reference against this application. It is respectfully submitted that this ground of rejection should be withdrawn.

As stated in the December 22, 2003 Amendment, the inventions described in the application are co-owned by the Board of Supervisors of Louisiana State University and Agricultural and Mechanical College ("LSU") and the Universidad de Alcalá of Madrid, Spain. The subject matter of the claims were commonly owned at the time the inventions were made. The co-inventors have an obligation to assign their inventions to at least one of the above named co-owners.

Conclusion

If any issues arise that may present an obstacle to allowance, the undersigned would welcome a telephone call to discuss such matters before further action is taken. Otherwise, allowance of Claims 1-10 at an early date is respectfully requested.

Respectfully submitted,

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